

REMARKS

Summary of Claim Amendments

After amended herein, claims 2-3, 11, 13-20, 25, 29-30, 32, 34-49, 51-64 and 68-104 are currently pending in the application, with claims 15, 16, 18-20, 25, 36 and 37 being withdrawn. Claims 4-6, 28, 31, 33, 50 and 65-67 have been cancelled.

Claim 2 has been amended to remove the representation that Z “represents a saturated or unsaturated, substituted or unsubstituted, straight-chain or branched C₄ - C₁₈ hydrocarbon group in which the C-24 or equivalent position is hydroxylated” and the side chain of formula IIB has been added. Basis for this amendment can be found on pages 9-12 of the specification. Claim 3 has been amended to remove the representation that Z “represents a saturated or unsaturated, substituted or unsubstituted, straight-chain or branched C₄ - C₁₈ hydrocarbon group in which the C-24 or equivalent position is hydroxylated” and the side chains of formula IIB, IID and IIF have been added. Basis for this amendment can be found on pages 9-14 of the specification. Claim 11 has been amended to be drawn to a 24-hydroxyvitamin D compound of formula I and side chain formula IIB, IID or IIF. Basis for this amendment can be found on page 9-12 of the specification. Claim 13 has been amended to be directed towards a 24-hydroxyprevitamin D compound of formula III and side chain formula IIB, IID or IIF. Basis for this amendment can be found on page 9-13 of the specification. Claim 14 has been amended to be directed towards a 24-hydroxyvitamin D compound of formula I and side chain formula IIB, IID or IIF. Basis for this amendment can be found on page 9-12 of the specification.

Claim 29 has been amended to be directed toward the side chain formula IIB. Basis for this amendment can be filed in the originally filed claim. Claim 32 has been amended to be directed towards the side chain formula IID. Basis for this amendment can be found in the originally filed claim. Claim 34 has been amended to depend from claim 32 and to relate solely to 24-OH-25-ene-*preD*₂. Claim 51 has been amended to be directed to 24-hydroxyprevitamin D₂. Basis for this amendment can be found in pages 9-12 of the specification. Claim 68 has been amended to be directed towards 24-hydroxyprevitamin D₂. Basis for this amendment can be found on pages 2-14 of the specification. Claims 87-90 have been added to claims specific 24 hydroxyvitamin D formulations which are used in the methods of claim 14. Basis for these

claims are found on pages 9-14 of the specification. Claims 91-104 have been added to relate to a method of treating a human to alleviate the pathological effects of various disease states by using a 24-hydroxyprevitamin D of formula III and side chain formula IIB, IID or IIF. Basis for these claims can be found on pages 9-14 of the specification. Applicants respectfully submit that no new matter has been added by these amendments.

Summary of pending claims

Claim 2 of the application relates to a method of achieving an effect in a patient comprising administering a 24-hydroxyvitamin D of formula I having a side chain of formula IIB, wherein the effect is treating bone loss or bone mineral content, hyperparathyroidism, hyperproliferation, or modulating the immune or inflammatory response. Claims 17, 35 and 38-44 depend directly or indirectly from claim 2.

Claim 3 of the application relates to a method of achieving an effect in a patient comprising administering a 24-hydroxyprevitamin D of formula III having side chains of formula IIB, IID or IIF, wherein the effect is treating bone loss or bone mineral content, hyperparathyroidism, hyperproliferation, or modulating the immune and inflammatory responses. Claims 29-30, 32, 34, 46-49 and 50 depend directly or indirectly on claim 3.

Claim 11 of the application relates to a method of achieving an effect in a patient comprising administering a 24-hydroxyvitamin D of formula I having side chains of formula IIB, IID or IIF, wherein the effect is increasing or maintaining bone mass or bone mineral content, lowering or maintaining lowered parathyroid hormone level, inhibiting hyperproliferative effects, inducing or enhancing cell differentiation or modulating inflammatory response. Claims 52-59 depend directly or indirectly on claim 11.

Claim 13 of the application relates to a method of achieving an effect in a patient comprising administering a 24-hydroxyprevitamin D of formula III having side chains of formula IIB, IID or IIF, wherein the effect is increasing or maintaining bone mass or bone mineral content, lowering or maintaining lowered parathyroid hormone level, inhibiting hyperproliferative effects, inducing or enhancing cell differentiation or modulating inflammatory response. Claims 60-64 and 68 depend directly or indirectly on claim 13.

Claim 14 of the application relates to a method of treating a human to alleviate the pathological effects of osteoporosis, hyperparathyroidism, psoriasis, skin cancer, breast cancer, colon cancer, prostate cancer, prostatic hyperplasia, or inflammatory response imbalance comprising administering a 24-hydroxyvitamin D of formula I having side chains of formula IIB, IID or IIF. Claims 69-90 depend directly or indirectly from claim 14.

Claim 91 of the application relates to a method of treating a human to alleviate the pathological effects of osteoporosis, hyperparathyroidism, psoriasis, skin cancer, breast cancer, colon cancer, prostate cancer, prostatic hyperplasia, or inflammatory response imbalance comprising administering a 24-hydroxy*previtamin* D of formula III having side chains of formulas IIB, IID or IIF. Claims 92-104 depend directly or indirectly from claim 14.

Interview with the Examiner

Applicants wish to thank the Examiner for the courtesy extended to them in the July 13, 2004 interview. In the interview we discussed with the Examiner that a terminal disclaimer had already been filed to overcome the obviousness double patenting rejection with respect to U.S. Patent No. 6,242,434. During the interview, the Examiner confirmed that the terminal disclaimer was in the image file wrapper. We also discussed with the Examiner limiting the claims to 24-hydroxyvitmain D and 24-hydroxy*previtamin* D formulations where the side chain only contains a hydroxyl group in the C-24 position.

Response to claim rejections

Claims 2-6, 11, 13, 14, 17, 28-35 and 35-86 currently stand variously rejected. Claims 2, 5, 28, 31 and 38 stand objected to for a variety of informalities. Claims 2, 3, and 13 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Claims 2-6, 11, 13, 14, 17, 28-35 and 38-86 stand rejected under the judicially created doctrine of double patenting over U.S. Patent No. 6,242,434. Claims 2-6, 11, 13, 14, 17, 28-35 and 38-86 stand rejected over 35 U.S.C. § 103(a) over U.S. Patent Reissue 36,854 issued to Sestelo et al. (hereinafter “Sestelo”). Applicants traverse these rejections for at least the following reasons.

Objections to the claims

Claims 4, 28 and 38 have been objected to as failing to define (m). Applicants point out that claim 38 does not contain a substituent (m) and claims 4 and 28 have been cancelled, rendering this objection moot.

Claim 5 has been objected to as depending on a subsequently numbered claim. As claim 5 has been cancelled, this objection has been rendered moot.

Claim 31 has been objected to as failing to exclude the parenthesis. As claim 31 has been cancelled, this objection has been rendered moot.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 2, 3, and 13 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. The Examiner asserts that the term “equivalent” in claims 2, 3 and 13 have rendered the claims indefinite. Claims 2, 3 and 13 have been amended to remove this language. Applicants respectfully request that the Examiner withdraw the rejections to claims 2, 3, and 13 on this ground.

Double patenting Rejection over U.S. Patent No. 6,242,434

Claims 2-6, 11, 13, 14, 17, 28-35 and 38-86 stand rejected under the judicially created doctrine of double patenting over U.S. Patent No. 6,242,434. Applicants respectfully submit that they addressed this rejection in the response, filed February 20, 2004, to the last Office Action. Along with the previous response, Applicants submitted a terminal disclaimer with respect to U.S. Patent No. 6,242,434. A copy of the previously filed terminal disclaimer is submitted herewith as requested by the Examiner in the interview of July 13, 2004. Applicants respectfully request that as a properly filed terminal disclaimer to U.S. Patent No. 6,242,434 has been filed, the Examiner withdraw the rejections to the claims on this ground.

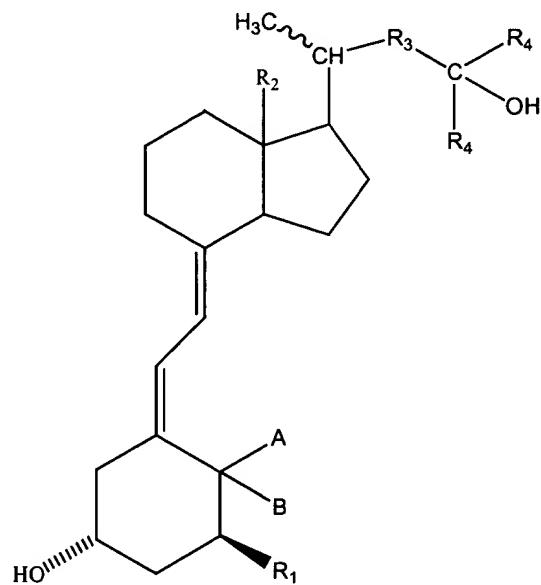
Rejections under 35 U.S.C. § 103(a) over Sestelo

Claims 2-6, 11, 13, 14, 17, 28-35 and 38-86 stand rejected over 35 U.S.C. § 103(a) over Sestelo. Applicants respectfully submit that the Office Action has failed to put forth a *prima*

facie case of obviousness with respect to these claims as Sestelo fails to teach or suggest all of the limitations of the claims.

Claims 2, 3, 11, 13, 14 and 91 upon which the other claims depend, all are drawn to methods utilizing a 24-hydroxyvitamin D or a 24-hydroxyprevitamin D where the only hydroxyl group that occurs in the side chain of the compounds is at the C-24 position. No hydroxyl groups are present at the terminal carbon of the side chains of the presently claimed vitamin D and previtamin D compounds.

In contrast, the Sestelo reference discloses vitamin D compounds which always have a hydroxyl group on the terminal carbon of the side chain. Sestelo discloses a vitamin D formulation of formula I:



wherein "R₃ is a branched or non-branched, saturated or unsaturated aliphatic 3- to 5-membered hydrocarbon or oxahydrocarbon biradical, having at least 3 atoms in the main chain and being optionally substituted with one or more substituents selected from epoxy, fluoro and hydroxyl." See col. 2, lines 5-33 of Sestelo. Sestelo, therefore, discloses vitamin D compounds wherein when the C-24 position is hydroxylated, the side chain contains at least two hydroxyl groups, one in the C-24 position, and the other in the terminal carbon position. The Sestelo patent contains no teaching or suggestion of any vitamin D or previtamin D compound that has a monohydroxylated side chain in the C-24 position.

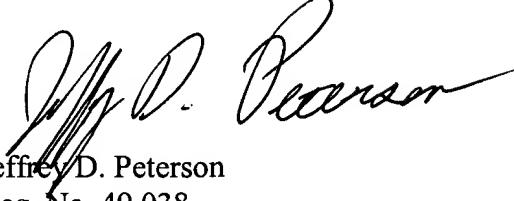
As is discussed in the present application, active vitamin D compositions are associated with toxicity and can be unpredictable in their effect when changes are made to the compound. See pages 1-5 of the specification. Nowhere does Sestelo disclose or even suggest that the side chain of its compounds can be modified to eliminate the terminal hydroxy and achieve the patented results. In fact, a careful reading of Sestelo would suggest that the terminal hydroxy group is a key aspect of Sestelo's patented invention. One of skill in the art would not have predicted or reasonably expected that a side chain, limited to a single hydroxyl group in the C-24 would be effective to treat Sestelo's disclosed disorders. Thus, there is no reasonable basis on the present record that provides a teaching or suggestion of applicant's claimed invention as noted in claims 2-6, 11, 13, 14, 17, 28-35 and 38-86.

Applicants respectfully submit that Sestelo fails to teach or suggest all of the limitations of claimed method. Absent any suggestion of Applicant's claimed method, the factual predicate necessary to establish a *prima facie* case of obviousness has not been met. Applicants therefore respectfully request that the rejections to these claims be withdrawn.

SUMMARY

Based on the foregoing, Applicants respectfully submit that the present application is in condition for allowance, and a favorable action thereon is respectfully requested. Should the Examiner feel that any other point requires consideration or that the form of the claims can be improved, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,



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